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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,535	10/12/2005	Josef Prassler	MS027US	8828

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EXAMINER	
VOGEL, NANCY TREPTOW	
ART UNIT	PAPER NUMBER
1636	

NOTIFICATION DATE	DELIVERY MODE
05/14/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/522,535	PRASSLER ET AL.	
	Examiner	Art Unit	
	NANCY VOGEL	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lohning (US2002/0034733) in view of Burger et al. (Appl. Microbiol. Biotechnol. (1999) 52:345-353).

This rejection is maintained essentially for the reasons made of record in the previous Office action, mailed 11/3/09. To recapitulate,

Lohning disclose phagemid vectors [0010] comprising a prokaryotic promoter (Fig. 16a) , a first nucleic acid sequence encoding an immunoglobulin-presenting polypeptide, which may be the phage coat protein gIII [0015] or fragment thereof [0017], a second nucleic acid sequence encoding a first Ig polypeptide, and a third nucleic acid sequence encoding a second Ig polypeptide [0050]. See Figs. 6a, 7a, 16a. A first and second associating agent are fused to or comprised within said Ig-presenting polypeptide and the first Ig polypeptide [0008, 0009, 0010]. The reference discloses that the first and second Ig polypeptides self-associate to form a Fab or other functional Ig fragment, via non-covalent interactions [0156]. The reference discloses that the first and second associating agents associate with each other via disulfide bond, and is a cysteine residue [0054]. The reference discloses prokaryotic secretory

signal sequences in the same reading frame as each of the nucleic acid sequences [0156-0157]. The associating agents would become disassociated in solution upon the addition of a reducing agent [0070]. The vector comprises a ribosome binding site positioned 5' to the nucleic acid sequence encoding each of the first, second and third polypeptide, since it is shown in the reference that proteins are produced using the disclosed expression vectors, and therefore at least one ribosome binding site is present in the normal, 5' region of the start site of the polypeptide encoding region. The reference exemplifies the use of two vectors, with one encoding the Ig presenting polypeptide pIII, and a bicistronic vector encoding the heavy and light chain, with each comprising a signal sequence upstream of the coding region , wherein the resultant Fab is linked to the pIII protein via disulfide bond (Example 2.2). The difference between the reference and the instant claims is that a single tricistronic vector carrying all components is not disclosed.

However, tricistronic vectors are known in the art as disclosed by Burger et al. Burger et al. disclose tri-cistronic vectors to achieve stable expression and/or secretion of three polypeptides of interest, two of which are Ig polypeptides (light chain and heavy chain). The reference discloses that a tricistronic vector is useful for "providing stability of expression which is a critical requirement for industrial scale production" (page 351). It would have been obvious to one of ordinary skill in the art to have used a tricistronic vector, as disclosed by Burger et al., to express the genes disclosed by Lohning, since both references are concerned with the expression of three different gene products simultaneously in an expression system. One would have been motivated to do so by

the disclosure of Burger et al. of the usefulness of such vectors for obtaining stability of expression of three gene products. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention. Applicants have argued in their response filed 9/3/09 that the rejection should be withdrawn, since Burger et al. had difficulties in expressing two structural proteins using the disclosed tricistronic vector, and Burger et al. used the tricistronic vector for a "completely different purpose than the present application, the creation of a cell line for large scale production", and therefore there is no motivation to combine the references. Applicants point to page 348 of Burger et al. to support the argument that there were difficulties encountered in the expression of only two structural polypeptides, and puromycin acetyltransferase, which is an enzyme that allows selection due to puromycin resistance. However, while Burger may have disclosed that there were difficulties encountered, it remains that Burger et al. was successful in the expression of three proteins. The fact that one of the proteins was not a "structural" protein as opposed to an enzyme, does not obviate the fact that Burger et al. succeeded in using a tricistronic vector for the expression of three encoded proteins or enzymes. Furthermore, applicants argue that Burger et al. used the tricistronic vector for a completely different purpose, since their goal was the production of a high yield, stable cell line, as opposed to a phage display of proteins. However, it is maintained that the high expression of the encoded three proteins was a common goal in both Burger et al. and the instant application, and the fact that different proteins were encoded does not

teach away from the combination of the references. One of ordinary skill in the art would have recognized that a vector for the expression of any particular proteins, would be applicable to the expression of different proteins, since gene expression using any particular vector is well known in the art. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention. Therefore, the rejection is maintained.

Applicant's arguments filed 1/28/10 have been considered but have not been found convincing.

Applicants have argued that in the interview of 1/27/10 the "Examiner agreed that the Burger et al. reference does not serve as a basis for a 103(a) rejection, and therefore, applicant respectfully requests that this rejection be withdrawn". Furthermore, the applicant states that in the RCE filed on 9/3/09, certain statements regarding the Burger et al. reference were made which were in error and without intent to deceive the Examiner. Applicant state that clones 3-1, 3-2 and 3-3 were generated using monocistronic vectors, not tricistronic vectors. Only clone 1-8, of the clones discussed by the applicant, was a tricistronic vector. The examiner has further reviewed the Burger et al. reference in view of these statements, and concluded that Burger et al. actually teaches that the tri-cistronic vector (clones 1-2, 1-6, 1-7, 1-8 in Fig. 2), other than clone 1-8 which does not appear to produce any tri-cistronic RNA product or protein product, produces the highest level of IgG product in the supernatant. Burger et

al. concludes that "Levels of IgG in supernatant ...and intense high-molecular-weight IgG Western blot bands (possibly consistent with full-size hc-lc fusion product) identified the tri-cistronic transfectants as the option most likely to deliver an appropriate production cell line" (page 348, second col.). This conclusion leads one to conclude that tri-cistronic vectors are preferable to bi- or mono- cistronic expression of three polypeptides. Therefore, in view of this consideration of Burger et al., applicant's arguments are not found convincing and the rejection is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NANCY VOGEL whose telephone number is (571)272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/
Primary Examiner, Art Unit 1636

NV
5/8/10